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NOTIFICATION OF ELECTION

(PCT Rule 61.2)

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Date of mailing (day/month/year) 26 February 1999 (26.02.99)	Applicant's or agent's file reference L0461/7039WO
International application No. PCT/US98/14679	Priority date (day/month/year) 17 July 1997 (17.07.97)
International filing date (day/month/year) 15 July 1998 (15.07.98)	
Applicant SCANLAN, Matthew, J. et al	

1. The designated Office is hereby notified of its election made:



in the demand filed with the International Preliminary Examining Authority on:

20 January 1999 (20.01.99)



in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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			(43) International Publication Date: 28 January 1999 (28.01.99)
(21) International Application Number: PCT/US98/14679			
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(30) Priority Data:			
08/896,164	17 July 1997 (17.07.97)	US	
60/061,599	10 October 1997 (10.10.97)	US	
60/061,765	10 October 1997 (10.10.97)	US	
08/948,705	10 October 1997 (10.10.97)	US	
9721697.2	11 October 1997 (11.10.97)	GB	
09/102,322	22 June 1998 (22.06.98)	US	
(71) Applicant (for all designated States except US): LUDWIG INSTITUTE FOR CANCER RESEARCH [CH/US]; 605 Third Avenue, New York, NY 10158 (US).			
(72) Inventors; and			
(75) Inventors/Applicants (for US only): OLD, Lloyd, J. [US/US]; 1345 Avenue of the Americas, New York, NY 10105 (US). SCANLAN, Matthew, J. [US/US]; 1275 York Avenue, New York, NY 10021 (US). STOCKERT, Elisabeth [US/US]; 1275 York Avenue, New York, NY 10021 (US). GURE, Ali [TR/US]; 1275 York Avenue, New York, NY 10021 (US). CHEN, Yao-Tseng [-/US]; The New York Hospital-Cornell Medical Center, Dept. of Pathology, 525 East 68th Street, New York, NY 10021 (US). GOUT, Ivan			
		(74) Agent: VAN AMSTERDAM, John, R.; Wolf, Greenfield & Sacks, P.C., 600 Atlantic Avenue, Boston, MA 02210 (US).	
		(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).	
		Published Without international search report and to be republished upon receipt of that report.	
(54) Title: CANCER ASSOCIATED NUCLEIC ACIDS AND POLYPEPTIDES			
HY-10-12 KENSPPPTKVVHPLIGLILEYGGSDNYEEELKQTPPPQPIITAQPKREEQTKKENZEKLTDMKILACLICRRQPPHKEVL 970			
LUCA15	PRIVKNGDEE(PKRGGLVAAVSGSDNHEE.....	ELVERLESEHEKILADWKKMACLLCRRQPPHKOAL	662
IXS8237E	DLPKLASDDHPPPTGLVAAVSGSDNHEE.....	EDERGPFEREKLTWOKLACLICRRQPPSKEAL	233
HY-10-12 TIIHQQLSDLIKQNHLEIHRKTKQSEKLAYLERRERE..GIFKGRHNDREKLSQSPDPERKRIKYSRETD..DRKLVKEDID 1050			
LUCA15	VRIHQQLSDLIKQNHLEIHRKTKQSEKLAYLERRERE..MKYRDRAERREKYGIEPPEPPEKKEKQFAGTV...NYEQPTKDGID	742	
IXS8237E	TDHQQLSGLIKQNHLEIHRKTKQSEKLAYLERRERE..MKYRDRAERREKYGIEPPEPPEKKEKQFAGTV...NYEQPTKDGID	316	
HY-10-12 TISKQCVVQATGHRGTGIGYHPIGLASCHAEGRNRGSPVGAAGTSSKRQSHETIRDAVRVVMFARYKELD 7123			
LUCA15	HSNICHKILQAHGWRGSGLGRIUQGITAPTEAQVLLKAGLAKGSAATGLSGADSYKDAVRKAMFARYTENE	815	
IXS8237E	SINIGSRHILQAHGWRGSGLGRIUQGITAPTEAQVLLKAGLAKGSAATGLSGADSYKDAVRKAMFARYTENE	389	
(57) Abstract			
Various molecules associated with cancer are disclosed. The invention also discloses diagnostic and therapeutic methods based upon these molecules.			



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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : C12N 15/12, C07K 14/705, C12Q 1/68, G01N 33/53, C07K 16/28, A61K 38/17, 31/70, 39/00, 35/12, 39/395, 48/00		A3	(11) International Publication Number: WO 99/04265
			(43) International Publication Date: 28 January 1999 (28.01.99)
(21) International Application Number: PCT/US98/14679		[UA/GB]; 91 Riding House Street, London W1P 8BT (GB). O'HARE, Michael [GB/GB]; 91 Riding House Street, Lon- don W1P 8BT (GB). OBATA, Yuichi [JP/JP]; Chikusa-Ku, Nagoya 464 (JP). PFREUNDSCHUH, Michael [DE/DE]; Innere Medizin 1, D-66421 Homburg/Saar (DE). TURECI, Ozlem [DE/DE]; Innere Medizin 1, D-66421 Homburg/Saar (DE). SAHIN, Ugur [TR/DE]; Innere Medizin 1, D-66421 Homburg/Saar (DE). (74) Agent: VAN AMSTERDAM, John, R.; Wolf, Greenfield & Sacks, P.C., 600 Atlantic Avenue, Boston, MA 02210 (US). (81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims</i> <i>and to be republished in the event of the receipt of amendments.</i>	
(22) International Filing Date: 15 July 1998 (15.07.98)			
(30) Priority Data: 08/896,164 17 July 1997 (17.07.97) US 60/061,599 10 October 1997 (10.10.97) US 60/061,765 10 October 1997 (10.10.97) US 08/948,705 10 October 1997 (10.10.97) US 9721697.2 11 October 1997 (11.10.97) GB 09/102,322 22 June 1998 (22.06.98) US			
(71) Applicant (for all designated States except US): LUDWIG INSTITUTE FOR CANCER RESEARCH [CH/US]; 605 Third Avenue, New York, NY 10158 (US).			
(72) Inventors; and (75) Inventors/Applicants (for US only): OLD, Lloyd, J. [US/US]; 1345 Avenue of the Americas, New York, NY 10105 (US). SCANLAN, Matthew, J. [US/US]; 1275 York Avenue, New York, NY 10021 (US). STOCKERT, Elisabeth [US/US]; 1275 York Avenue, New York, NY 10021 (US). GURE, Ali [TR/US]; 1275 York Avenue, New York, NY 10021 (US). CHEN, Yao-Tseng [-/US]; The New York Hospi- tal-Cornell Medical Center, Dept. of Pathology, 525 East 68th Street, New York, NY 10021 (US). GOUT, Ivan			
(54) Title: CANCER ASSOCIATED NUCLEIC ACIDS AND POLYPEPTIDES		(88) Date of publication of the international search report: 26 August 1999 (26.08.99)	
(57) Abstract			

Tumor cell-specific antigens from melanoma cells have previously been identified using autologous cytolytic T cells clones from the patient, but the same approach did not work well with other tumour types. Here, screening of such antigens was successfully performed using antisera from the patient. Provided are several tumor cell-specific antigens, nucleic acids encoding them, antibodies and CTL's directed against these antigens, antigenic fragments diagnostic kits, etc.

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/JP 98/14679

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C12N15/12 C07K14/705 C12Q1/68 G01N33/53 C07K16/28
 A61K38/17 A61K31/70 A61K39/00 A61K35/12 A61K39/395
 A61K48/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C12N C07K A61K G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
X	<p>WO 97 17470 A (HOLLAND JAMES F) 15 May 1997</p> <p>Also against claims 82-84, 116, 117 see whole document, particularly the claims</p> <p style="text-align: center;">---</p> <p style="text-align: center;">-/-</p>	<p>1,2, 4-10, 18, 21-23, 27, 28, 31, 32, 40, 42, 44, 45, 48-51, 58-60, 67-70, 76-79</p>

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *Z* document member of the same patent family

Date of the actual completion of the international search

3 June 1999

Date of mailing of the international search report

29. 06. 1999

Name and mailing address of the ISA

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/... 98/14679

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
X	GB 2 273 099 A (ASTA MEDICA AG) 8 June 1994 Also against claims 108,109,116,117. See whole document, particularly the claims and examples. ---	1,2, 4-10,31, 32,40, 42,43, 49,50, 58-60, 67,69, 71,72, 74-79, 82-84, 99-104
X	WO 97 17441 A (KISHIMURA MASAOKI ;OSAKADA FUMIO (JP); OSAKI SHOICHI (JP); NAKAO K) 15 May 1997 see the whole document -& EP 0 869 176 A (KANEKA CORPORATION, OSAKA, JAPAN) 7 October 1998 Also against claims 68-72,74,76,77,82,116,117 see claims 10,12; examples 2,5 ---	1,2,4-8, 13,18, 21,22, 24, 27-29, 31,32, 35,40, 42,44, 45, 47-50, 54,59, 60,63,67
X	WO 97 02362 A (FOX CHASE CANCER CENTER) 23 January 1997 see the whole document, particularly the claims and seq. 1 and 2. Also against claims 70-72,74,76-80,82-85,88,89,99-104,108-111, 116,117. see page 18, line 20 - page 22, line 33 ---	1,2, 4-10,15, 18, 21-24, 27-29, 31,32, 37,40, 42-45, 47-50, 56, 58-60, 65,67

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/ 98/14679

C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>VAUGHAN, J.H. ET AL.: "Epstein-Barr virus-induced autoimmune responses." JOURNAL OF CLINICAL INVESTIGATION, vol. 95, no. 3, March 1995, pages 1306-15. XP002103180</p> <p>see the whole document -& DATABASE EMBL - EMHUM1 Entry HSIGGAUA, Acc.no. L38696, 17 February 1995 VAUGHAN, J.H. ET AL.: "Homo sapiens autoantigen p542 mRNA, complete cds." XP002103198 see the whole document</p>	<p>1,2,18, 21,22, 24, 27-29, 31,35, 40,44, 45, 47-50, 54,59, 60,63, 67-72, 74-80,82</p>
X	<p>MASHIMO, J. ET AL.: "Decrease in the expression of a novel TGF betal-inducible and ras-recision gene, TSC-36, in human cancer cells." CANCER LETTERS, vol. 113, March 1997, pages 213-9, XP002104545 see abstract</p>	<p>1,2, 4-10,13</p>
X	<p>MACHIELS, B.M. ET AL.: "Nuclear lamin expression in normal testis and testicular germ cell tumours of adolescents and adults." JOURNAL OF PATHOLOGY, vol. 182, no. 2, June 1997, pages 197-204, XP002104546 see abstract see page 198, left-hand column, paragraph 2</p>	<p>1,2, 4-10,15, 31,32, 37,40, 42,116, 117</p>
X	<p>COATES, P.J. ET AL.: "Identification of the antigen recognized by the monoclonal antibody BU31 as lamins A and C" JOURNAL OF PATHOLOGY, vol. 178, no. 1, January 1996, pages 21-9, XP002104547 see abstract</p>	<p>1,2, 4-10,15, 31,32, 37,40, 42,116, 117</p>

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INTERNATIONAL SEARCH REPORT

International Application No.

PC1, JS 98/14679

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	ZWIJSEN, A. ET AL.: "Characterization of a rat C6 glioma-secreted follistatin-related protein (FRP); cloning and sequencing of the human homologue." EUROPEAN JOURNAL OF BIOCHEMISTRY, vol. 225, no. 3, November 1994, pages 937-46, XP002103181 see page 945, right-hand column, paragraph 2-4; figure 3	18,21, 22,24, 27,28, 44,45, 47-50, 54,59, 60,63, 67-72, 74-80,82
X	MINEGISHI, M. ET AL.: "Structure and function of Cas-L, a 105 kD Crk-associated substructure-related protein that is involved in beta-1 integrin-mediated signaling in lymphocytes." JOURNAL OF EXPERIMENTAL MEDICINE, vol. 184, no. 4, 1 October 1996, pages 1365-75, XP002103183 also against claims 116 and 117 see figure 4	18, 21-23, 27-29, 31,32, 37,40, 44,45, 47-50, 56, 58-60, 65, 67-72, 74-80, 82-84
X	JIN, Y-J. ET AL.: "The 25-kDa FK506-binding protein is localized in the nucleus and associated with casein kinase II and nucleolin." PROC.NAT'L.ACAD.SCI.USA, vol. 90, August 1993, pages 7769-73, XP002104548 see the whole document	31,32, 35,40, 116,117
X	WO 96 15149 A (UNIV WASHINGTON) 23 May 1996 see page 23, line 2 - line 3	31,32, 37,40
X	WO 97 21729 A (SLOAN KETTERING INST CANCER) 19 June 1997 see page 3, line 24 - line 29 see page 6, line 27 - line 29; figure 3 see page 27, line 15 see page 28, line 27 - line 28	31,32, 37, 40-42, 116,117

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INTERNATIONAL SEARCH REPORT

International Publication No

PCT, 98/14679

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>NOCE, T. ET AL.: "Expresson of a mouse zinc finger protein gene in both spermatocytes and oocytes during meiosis." DEVELOPMENTAL BIOLOGY, vol. 153, no. 2, October 1992, pages 356-67, XP002104549 see abstract; figures 1,5-7 -& DATABASE EMBL - EMROD Entry MMZFP51, Acc.no. D10630, 8 November 1992 NOCE, T. ET AL.: "Mouse mRNA for zinc finger protein, complete cds." XP002104555 see the whole document</p> <p style="text-align: center;">---</p>	<p>31,32, 37,40, 42, 67-70, 116,117</p>
X	<p>ONO M ET AL: "NUCLEOTIDE SEQUENCE OF HUMAN ENDOGENOUS RETROVIRUS GENOME RELATED TO THE MOUSE MAMMARY TUMOR VIRUS GENOME" JOURNAL OF VIROLOGY, vol. 60, no. 2, 1 November 1986, pages 589-598, XP000673638 see page 597, left-hand column, paragraph 5 - right-hand column, paragraph 1; figure 1</p> <p style="text-align: center;">---</p>	<p>44,45, 47,48, 59,60, 67-72,74</p>
X	<p>DATABASE EMBL - EMBEST16 Entry HSC9958, Acc.no. C15995, 29 September 1996 FUJIWARA, T. ET AL.: "Human fetal brain cDNA 5'-end GEN-421G02." XP002103191 see the whole document</p> <p style="text-align: center;">---</p>	<p>44,59, 60,63, 67-70</p>
X	<p>DATABASE EMBL - EMBEST13 Entry HS570350, Acc.no. W45570, 27 May 1996 HILLIER, L. ET AL.: "zc26f08.s1 Soares senescent fibroblasts NbHSF Homo sapiens cDNA clone 323463 3'" XP002103192 see the whole document</p> <p style="text-align: center;">---</p>	<p>44,59, 60,63, 67-70</p>
X	<p>DATABASE EMBL - EMBEST15 Entry HSA07407, Acc.no. AA007407, 28 July 1996 HILLIER, L. ET AL.: "zh97b08.r1 Soares fetal liver spleen 1NFLS S1 Homo sapiens cDNA clone 429207 5'" XP002103193 see the whole document</p> <p style="text-align: center;">---</p>	<p>44,59, 60,63, 67-70</p>

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INTERNATIONAL SEARCH REPORT

International Application No

PCT, 98/14679

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>HUNG, D.T. ET AL.: "cDNA cloning of a human 25 kDa FK506 and rapamycin binding protein."</p> <p>BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, vol. 184, no. 2, 30 April 1992, pages 733-8, XP002103178 see figure 2</p> <p style="text-align: center;">---</p>	<p>44,59, 60,63, 67-70</p>
X	<p>JIN, Y-J. ET AL.: "Molecular cloning of a 25-kDa high affinity rapamycin binding protein, FKBP25."</p> <p>JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 267, no. 16, 5 June 1992, pages 10942-5, XP002104550 see figure 3</p> <p style="text-align: center;">---</p>	<p>44, 47-50, 54,59, 60,63, 67-72, 75,83,84</p>
X	<p>MACLEOD, A.R. ET AL.: "A muscle-type tropomycin in human fibroblasts: evidence for expression by an alternative RNA splicing mechanism."</p> <p>PROC.NAT'L.ACAD.SCI.USA, vol. 82, December 1985, pages 7835-9, XP002103179 see figures 2,3</p> <p style="text-align: center;">---</p>	<p>44,59, 60,63, 67-70</p>
X	<p>DATABASE EMBL - EMBEST20 Entry/Acc.no. T09468, 8 August 1993 ADAMS, M.D. ET AL.: "EST07361 Homo sapiens cDNA clone HIBBU63 5' end." XP002103195 see the whole document -& ADAMS, M.D. ET AL.: "Rapid DNA sequencing (expressed sequence tags) from a directionally cloned human infant brain cDNA library." NATURE GENETICS, vol. 4, 1993, pages 373-380, XP000574910 see the whole document</p> <p style="text-align: center;">---</p>	<p>44,45, 67,70</p>
X	<p>DATABASE EMBL - EMBEST17 Entry HSZZ32361, Acc.no. AA327309, 18 April 1997 ADAMS, M.D. ET AL.: "EST30621 Colon I Homo sapiens cDNA 5' end." XP002103199 see the whole document -& ADAMS, M.D. ET AL.: "Initial assessment of human gene diversity and expression patterns based upon 83 million nucleotides of cDNA sequence." NATURE, vol. 377, 1995, pages 3-17, XP002042918 see the whole document</p> <p style="text-align: center;">---</p>	<p>44,45, 60,62, 67,70</p>

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INTERNATIONAL SEARCH REPORT

International Application No

PCT, 98/14679

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE EMBL - EMBEST15 Entry HSAA33416, Acc.no. AA133416, 6 December 1996 HILLIER, L. ET AL.: "zk96e08.r1 Soares pregnant uterus NbHPU Homo sapiens cDNA clone 490694 5'." XP002103196 see the whole document</p>	44,45, 67,70
X	<p>--- DATABAS EMBL - EMBEST11 Entry HS1282878, Acc.no. AA487071, 28 June 1997 HILLIER, L. ET AL.: "ab18f11.s1 Stratagene lung (#937210) Homo sapiens cDNA clone 841197 3' similar to contains Alu repetitive element." XP002103197 see the whole document</p>	44,45, 67,70
X	<p>--- DATABAS EMBL - EMBEST15 Entry HSAA21198, entry AA121198, 21 November 1996 HILLIER, L. ET AL.: "z188g08.r1 Stratagene colon (#937204) Homo sapiens cDNA clone 511742 5'." XP002103200 see the whole document</p>	44,45, 60,62, 67,70
X	<p>--- DATABAS EMBL - EMBEST15 Entry HSAA21174, Acc.no. AA121174, 21 November 1996 HILLIER, L. ET AL.: "z188g08.s1 Stratagene colon (#937204) Homo sapiens cDNA clone 511742 3'." XP002103202 see the whole document</p>	44,45, 60,62, 67,70
X	<p>--- DATABAS EMBL - EMBEST17 Entry HSW22160, Acc.no. W22160, 9 May 1996 NATHANS, J.: "63A6 Human retina cDNA Tsp509I-cleaved sublibrary Homo sapiens cDNA not directional." XP002103201 see the whole document</p>	44,45, 60,62, 67,70
X	<p>--- DATABAS EMBL - EMBEST15 Entry HSA29201, Acc.no. AA029201, 20 August 1996 HILLIER, L. ET AL.: "zk12f08.s1 Soares pregnant uterus NbHPU Homo sapiens cDNA clone 470343 3'." XP002103203 see the whole document</p>	44,45, 60,62, 67,70

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INTERNATIONAL SEARCH REPORT

International Application No

PCT, 98/14679

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE EMBL - EMBEST17 Entry HSW29097, Acc.no. W29097, 14 May 1996 NATHANS, J.: "56d11 Human retina cDNA randomly primed sublibrary Homo sapiens cDNA." XP002103204 see the whole document</p> <p>---</p>	<p>44,45, 60,62, 67,70</p>
X	<p>MIKI Y ET AL: "A STRONG CANDIDATE FOR THE BREAST AND OVARIAN CANCER SUSCEPTIBILITY GENE BRCA1" SCIENCE, vol. 266, no. 12, 7 October 1994, pages 66-71, XP000202410 see the whole document -& DATABASE EMBL - EMBEST5 Entry/Acc.no. AF039241, 17 January 1998 MIKI, Y. ET AL.: "Homo sapiens clone 11-67js mRNA,partial sequence." XP002103205 see the whole document</p> <p>---</p>	<p>44,45, 60,62, 67,70</p>
X	<p>DATABASE EMBL - EMBEST18 Entry MM1140465, Acc.no. AA221749, 15 February 1997 MARRA, M. ET AL.: "my28g01.r1 Barstead mouse pooled organs MPLRB4 Mus musculus cDNA clone 697200 5' similar to TR:E239664 E239664 CHROMOSOME XIV READING FRAME ORF YNL021W." XP002103206 see the whole document</p> <p>---</p>	<p>44,45, 60,62, 67,70</p>
X	<p>NAGASE T ET AL: "PREDICTION OF THE CODING SEQUENCES OF UNIDENTIFIED HUMAN GENES VI.THE CODING SEQUENCES OF 80 NEW GENES (KIAA0201-KIAA0280) DEDUCED BYANALYSIS OF CDNA CLONES FROM CELL LINE KG-1 AND BRAIN" DNA RESEARCH, vol. 3, no. 5, 1 January 1996, pages 321-329, XP002059454 see the whole document -& DATABASE EMBL - EMHUM1 Entry HSD455, Acc.no. D87455, 9 November 1996 NOMURA, N.: "Human mRNA for KIAA0266 gene, complete cds." XP002103207 see the whole document</p> <p>---</p>	<p>44,45, 60,62, 67,70</p>

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INTERNATIONAL SEARCH REPORT

International Application No.

PCT, J 98/14679

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE EMBL - EMBEST16 Entry HSAA51187, Acc.no. AA151187, 15 December 1996 HILLIER, L. ET AL.: "zo03c11.r1 Stratagene colon (#937204) Homo sapiens cDNA clone 566612 5'." XP002103208 see the whole document ---</p>	<p>44,45, 60,62, 67,70</p>
X	<p>DATABASE EMBL - EMHUM2 Entry HSU50839, Acc.no. U50839, 9 March 1997 LATIF, F. ET AL.: "Homo sapiens g16 protein (g16) mRNA, complete cds." XP002103209 see the whole document ---</p>	<p>44,45, 60,64, 67,70</p>
X	<p>LI, H. ET AL.: "Isolation and sequence analysis of the human syntaxin-encoding gene." GENE, vol. 143, 1994, pages 303-4, XP002103182 see the whole document ---</p>	<p>44,45, 47,48, 59,60, 65, 70-72, 74,83,84</p>
X	<p>DATABASE EMBL - EMBEST11 Entry HS1188646, Acc.no. AA285170, 5 April 1997 STRAUSBERG, R.: "zs48f04.s1 NCI CGAP GCB1 Homo sapiens cDNA clone IMAGE:700735-3'." XP002103210 see the whole document ---</p>	<p>44,45, 59,60, 67-70</p>
X	<p>FISHER, D.Z. ET AL.: "cDNA sequencing of nuclear lamins A and C reveals primary and secondary structural homology to intermediate filament proteins." PROC.NAT'L.ACAD.SCI.USA, vol. 83, September 1986, pages 6450-4, XP002103184 see figure 2 ---</p>	<p>44,45, 59,60, 67-70</p>
X	<p>DATABASE EMBL - EMBEST16 Entry HSAA54222, Acc.no. AA454222, 11 June 1997 HILLIER, L. ET AL.: "zx48g12.s1 Soares testis NHT Homo sapiens cDNA clone 795526 3' similar to gb:D42040 RING3 PROTEIN (HUMAN)" XP002103189 see the whole document ---</p>	<p>67,69</p>

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INTERNATIONAL SEARCH REPORT

International Application No

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
X	<p>DATABASE EMBL - EMBEST11 Entry HS125289, Acc.no. AA454221, 11 June 1997 HILLIER, L. ET AL.: "zx48g12.r1 Soares testis NHT Homo sapiens cDNA clone 795526 5' similar to TR:E243068 E243068 KINASE." XP002103190 see the whole document</p> <p>---</p>	67,69
X	<p>DATABASE EMBL - EMBEST20 Entry MMAA84412, Acc.no. AA184412, 19 February 1997 MARRA, M. ET AL.: "mt34f07.r1 Soares mouse 3NbMS Mus musculus cDNA clone 622981 5' similar to SW:OXYB HUMAN P22059 OXYSTEROL-BINDING PROTEIN." XP002103194 see the whole document</p> <p>---</p>	67-70
A	<p>WO 96 29409 A (LUDWIG INST CANCER RES ;UNIV LEIDEN (NL)) 26 September 1996</p> <p>see the whole document</p> <p>---</p>	1-11, 17-33, 39-52, 58-61, 67-117
A	<p>WO 92 20356 A (LUDWIG INST CANCER RES) 26 November 1992</p> <p>see the whole document, particularly the claims</p> <p>---</p>	1-11, 17-33, 39-52, 58-61, 67-117
A	<p>WO 95 23874 A (LUDWIG INST CANCER RES) 8 September 1995 see page 5, line 10-14; claims 3,4,7; examples 33,36,43,44</p> <p>---</p>	1-4
A	<p>FRANZÉN, B. ET AL.: "Analysis of polypeptide expression in benign and malignant human breast lesions: down-regulation of cytokeratins." BRITISH JOURNAL OF CANCER, vol. 73, 1996, pages 1632-8, XP002104551 see abstract</p> <p>---</p>	1,2,4-9, 13
A	<p>WO 96 10413 A (LUDWIG INST CANCER RES) 11 April 1996 see the whole document, particularly the claims see abstract</p> <p>---</p>	3,19,20, 26,39

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INTERNATIONAL SEARCH REPORT

International Publication No

PCT, 98/14679

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Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	BOON T ET AL: "Tumor antigens recognized by T cells" IMMUNOLOGY TODAY, vol. 18, no. 6, June 1997, page 267-268 XP004068293 see the whole document ---	
A	SAHIN, U. ET AL.: "Human neoplasms elicit multiple specific immune responses in the autologous host." PROC.NATL.ACAD.SCI.USA, vol. 92, December 1995, pages 11810-3, XP002091914 cited in the application see the whole document ---	
P,X	DATABASE EMBL - EMHUM1 Entry/Acc.no. AC004022, 22 January 1998 HINDS, K. ET AL.: "Homo sapiens BAC clone GS155M11 from 7q21-q22, complete sequence." XP002091837 from nt.330-810 ---	1,2
P,X	ALAIYA, A.A. ET AL.: "Phenotypic analysis of ovarian carcinoma: polypeptide expression in benign, borderline and malignant tumors." JOURNAL OF CNACER, vol. 73, no. 5, 27 November 1997, pages 678-83, XP002104552 see abstract; figure 2 ---	1-10,15
P,X	GÜRE, A.O. ET AL.: "Human lung cancer antigens recognized by autologous antibodies: definition of a novel cDNA derived from the tumor suppressor gene locus on chromosome 3p21.3" CANCER RESEARCH, vol. 58, 1 March 1998, pages 1034-41, XP002103188 see the whole document ---	1,2,4,5, 9,14,18, 21,22, 27,44, 45,49, 50,55, 59,60, 64, 67-70, 83,84
P,X	SCANLAN, M.J. ET AL.: "Characterization of human colon cancer antigens recognized by autologous antibodies" INTERNATIONAL JOURNAL OF CANCER, 29 May 1998, pages 652-8, XP002103186 see the whole document ---	31,32, 34,40, 59,60, 62, 67-70, 83,84, 116

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INTERNATIONAL SEARCH REPORT

national Application No

PCT, 98/14679

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	<p>NAGASE, T. ET AL.: "Prediction of the coding sequence of unidentified human genes. IX. The complete sequence of 100 new cDNA clones from brain which can code for large proteins in vivo."</p> <p>DNA RESEARCH, vol. 5, 28 February 1998, pages 31-39, XP002103187 see figure 1; table 3 -& DATABASE EMBL Entry/acc.no. AB011172, 10 April 1998 NAGASE, T. ET AL.: "Homo sapiens mRNA for KIAA0600 protein, partial cds." XP002104556 see the whole document</p>	44,45, 67-70, 83,84
P,X	<p>---</p> <p>JONES, M.H. ET AL.: "Identification and characterization of BRDT: a testis-specific gene related to the bromodomain genes RING3 and Drosophila fsh."</p> <p>GENOMICS, vol. 45, no. 3, 1 November 1997, pages 529-34, XP002103185 see page 529, right-hand column, paragraph 2 see page 530, left-hand column, paragraph 2; figure 1 see page 532, right-hand column, paragraph 2</p>	44,45, 59,60, 67-70, 83,84
P,X	<p>---</p> <p>ISHIKAWA K ET AL: "Prediction of the coding sequences of unidentified human genes. X The complete sequences of 100 new cDNA clones from brain which can code for large proteins in vitro"</p> <p>DNA RESEARCH, vol. 5, no. 321, 30 June 1998, pages 169-176, XP002089186 see abstract; figures 1,2; table 2</p>	44,59, 60,63, 67-70
E	<p>---</p> <p>US 5 858 723 A (MUELLER-LANTZSCH NIKOLAUS ET AL) 12 January 1999</p> <p>Also against claims 108,109,116,117 see the whole document</p> <p>---</p>	1,2, 4-10,31, 32,40, 42,43, 49,50, 58-60, 67,69, 71,72, 74-79, 82-84, 99-104

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INTERNATIONAL SEARCH REPORT

International Application No

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E	<p>WO 98 40483 A (HUMAN GENOME SCIENCES INC ;GREENE JOHN M (US); LI YI (US); ROSEN C) 17 September 1998</p> <p>Also against claims 74,76-80,82-85,88,89, 99-104,108,109,111,116,117. See seq. 24 and the claims.</p> <p>---</p>	<p>1,2, 4-10,14, 18, 21-24, 27,28, 31,32, 36,40, 44,45, 47-50, 55, 58-60, 64,67-72</p>
E	<p>WO 98 08866 A (WISTAR INST) 5 March 1998 see the whole document</p> <p>---</p>	<p>1,2</p>
E	<p>WO 98 48015 A (CHUGAI RES INST MOLECULAR MED ;JONES MICHAEL H CHUGAI RESEARC (JP)) 29 October 1998</p> <p>see whole document, particularly the claims. & DATABASE WPI Derwent Publications Ltd., London, GB; AN 98-583658 XP002103211 see abstract</p> <p>---</p>	<p>18,22, 23, 27-29, 31,32, 40, 44-50, 58-60, 67-72, 74, 76-78, 85,88, 89,102, 103</p>
E	<p>WO 98 32853 A (GENETICS INST) 30 July 1998</p> <p>see seq. 7 and 8 see page 6, line 23 - page 8, line 12; claims 20-22 see page 21, line 17 - page 22, line 11</p> <p>---</p>	<p>18,21, 22,24, 27-29, 44,45, 47-50, 53,59, 60,62, 67-72, 74, 76-80,82</p>

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Intern: al Application No

PCT/US 98/14679

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
T	<p>SCANLAN, M.J. ET AL.: "Isoforms of the human PDZ-73 protein exhibit differential tissue expression" BIOCHIMICA ET BIOPHYSICA ACTA, vol. 1445, no. 1, 1999, pages 39-52, XP002104553 also for claims 77-80,82-84,116. see the whole document</p> <p style="text-align: center;">---</p>	
T	<p>DRABKIN, H.A. ET AL.: "DEF-3(g16/NY-LU-12), an RNA binding protein from the 3p21.3 homozygous deletion region in SCLC" ONCOGENE, vol. 18, 1999, pages 2589-97, XP002104554 see the whole document</p> <p style="text-align: center;">-----</p>	

INTERNATIONAL SEARCH REPORT

International application No.
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Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 85-111 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☒ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

1-14, 17-36, 39-55, 58-64, 67-117; see additional sheets, pages 3-4.
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1: claims 1-11,17-33,39-52,58-61,67-117,
all partially

The nucleic acid sequence of Seq.ID 1, fragments or complements thereof, and the corresponding polypeptide(s) encoded thereby, and immunogenic and/or HLA binding fragments thereof, optionally as part of a complex with a HLA molecule, an expression vector comprising said nucleic acid, and optionally a human HLA molecule, a host cell transformed with said vector, and an antibody against said polypeptide(s).

Also a method of diagnosing of a disorder characterised by overexpression of said polypeptide(s) and a method for determining regression, progression or onset of a disease associated with overexpression of said polypeptide(s), using agents that specifically bind to said nucleic acid, said polypeptide(s) or complexes of (fragments of) said polypeptide(s) and a HLA molecule. A kit comprising two polynucleotides for the detection of said nucleic acid
Also pharmaceutical preparations

- which enrich the presence of said polypeptide-HLA complex, optionally comprising an adjuvant, or
- which inhibits the expression of said polypeptide(s), or
- comprising an agent that selectively binds said polypeptide, optionally as a conjugate with a diagnostic or therapeutic compound, or
- comprising said nucleic acid, optionally in an expression vector, optionally in a host cell, or
- comprising said polypeptide(s), optionally in combination with an adjuvant, or
- comprising cytolytic T cells, specific for said polypeptide-HLA complex, or
- comprising an antibody against said polypeptide(s).

Inventions 2-119: claims 1-11,13,15,17-33,35,37,
39-52,54,56,58-61,63,65,67-117, all partially (1)

Inventions 2-119: Idem as subject 1 but limited to each of the DNA sequences as in Seq.ID:2-40,66,89-169 (odd numbers), 170,172,174, and 176-210, where invention 2 is limited to Seq.ID:2 and corresponding polypeptides encoded thereby, invention 3 is limited to Seq.ID:3 and corresponding polypeptides encoded thereby,....., and invention 119 is limited to Seq.ID:210 and corresponding polypeptides encoded thereby.

Invention 120: claims 1-10,13,17-32,35,
39-51,54,58-60,63,67-117, all partially

INVITATION TO PAY ADDITIONAL FEES

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Idem as subject 1 but limited to the DNA sequences seq.ID:211 and 329 and corresponding polypeptides encoded thereby.

Inventions 121-452: claims 1-10,13,16-32,35,38-51, 54,57-60,63,66-117, all partially (1)

Inventions 121-452: Idem as subject 1 but limited to each of the DNA sequences as in Seq.ID:212-328, and 330-543, where invention 121 is limited to Seq.ID:211 and corresponding polypeptides encoded thereby, invention 122 is limited to Seq.ID:212 and corresponding polypeptides encoded thereby,....., and invention 452 is limited to Seq.ID:543 and corresponding polypeptides encoded thereby.

Invention 453: claims 1-10,12,17-32,34,39-51,53, 58-60,62,67-117, all partially

Idem as subject 1 but limited to the DNA sequences seq.ID:544 and 554 and corresponding polypeptides encoded thereby.

Inventions 454 and 455: claims 1-10,12,17-32,34, 39-51,53,58-60,62,67-117, all partially

Inventions 454 and 455: Idem as subject 1 but limited to each of the DNA sequences as in Seq.ID:546 and 548, where invention 454 is limited to Seq.ID:546 and corresponding polypeptides encoded thereby, and invention 455 is limited to Seq.ID:548 and corresponding polypeptides encoded thereby.

Invention 456: claims 1-10,12,17-32,34,39-51,53, 58-60,62,67-117, all partially

Idem as subject 1 but limited to each of the DNA sequences as in Seq.ID:550, 552, 556, 558 and 560 and corresponding polypeptides encoded thereby.

Inventions 457-582: claims 1-10,12-14,17-32,34-36, 39-51,53-55,58-60,62-64,67-117, all partially (1)

Inventions 457-582: Idem as subject 1 but limited to each of the DNA sequences as in Seq.ID:562-586 (even numbers),

588-683,686,687,689,691,692,692, and 696-706, where invention 457 is limited to Seq.ID:562 and corresponding polypeptides encoded thereby, invention 458 is limited to Seq.ID:564 and corresponding polypeptides encoded thereby,....., and invention 582 is limited to Seq.ID:706 and corresponding polypeptides encoded thereby.

Invention 583: claims 1-10,14,17-32,36,39-51,55, 58-60,64,67-117, all partially

Idem as subject 1 but limited to each of the DNA sequences as in Seq.ID:707, 709, 711 and 712 and corresponding polypeptides encoded thereby.

Inventions 584-592: claims 1-117, all partially (1)

Inventions 584-592: Idem as subject 1 but limited to each of the DNA sequences as in Seq.ID:799-815 (odd numbers), where invention 584 is limited to Seq.ID:799 and corresponding polypeptides encoded thereby, invention 585 is limited to Seq.ID:801 and corresponding polypeptides encoded thereby,....., and invention 592 is limited to Seq.ID:815 and corresponding polypeptides encoded thereby).

For the sake of conciseness, the subject matter of the first invention is explicitly defined, the other subject matters are defined by analogy thereto.

(1) In as far as the claims searched for a group of inventions refer to specific groups of sequences, only those claims which refer to the groups comprising the nucleic acid sequence of a particular invention, and/or its corresponding polypeptide sequence(s), form parts of that invention.

Due to the fact that extensive sequence homologies were found between several groups of sequences during the additional searches, some of the sequences have been grouped, whereby each of these groups comprising two or more such homologous sequences is considered to be one invention.

Claims searched during primary and additional searches: 1-14,17-36,39-55,58-64,67-117, limited to:

Invention 1, seq.ID.1
Invention 52, seq.ID.111, and 112 (transl.)
Invention 61, seq.ID.129, and 130 (transl.)
Invention 71, seq.ID.149, and 150 (transl.)
Invention 72, seq.ID.151, and 152 (transl.)
Invention 116, seq.ID.206
Invention 120, seq.ID.211 and 329; (related sequences)
Invention 137, seq.ID.228
Invention 139, seq.ID.330

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Invention 219, seq.ID.411
Invention 453, seq.ID.544, and 545 (transl.),
and seq.ID.554, and 555 (transl.);
(related sequences)
Invention 454, seq.ID.546, and 547 (transl.)
Invention 455, seq.ID.548, and 548 (transl.)
Invention 456, seq.ID.550, and 551 (transl.),
and seq.ID.552, and 553 (transl.),
and seq.ID.556, and 557 (transl.),
and seq.ID.558, and 559 (transl.),
and seq.ID.560, and 561 (transl.);
(related sequences)
Invention 547 seq.ID.665
Invention 548, seq.ID.666
Invention 554, seq.ID.672
Invention 558, seq.ID.676
Invention 563, seq.ID.681
Invention 566, seq.ID.686
Invention 583, seq.ID.707, and 708 (transl.),
and seq.ID.709, and 710 (transl.),
and seq.ID.711,
and seq.ID.712;
(related sequences).

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT, JS 98/14679

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International Application No

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PATENT COOPERATION TREATY

PCT

REC'D 20 OCT 1999

WIPO PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference L0461/7039WO	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US98/14679	International filing date (day/month/year) 15/07/1998	Priority date (day/month/year) 17/07/1997
International Patent Classification (IPC) or national classification and IPC G01N33/574		
Applicant LUDWIG INSTITUTE FOR CANCER RESEARCH et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 8 sheets, including this cover sheet.

- ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 3 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☒ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 20/01/1999	Date of completion of this report 18. 10. 99
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer von Ballmoos, P Telephone No. +49 89 2399 8174 

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US98/14679

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1-88	as originally filed		
57a'-57b'	as received on	27/09/1999	with letter of 27/09/1999

Claims, No.:

1,2,3 (part), 9-117	as originally filed		
3 (part),4-8	as received on	27/09/1999	with letter of 27/09/1999

Drawings, sheets:

1/9-9/9	as originally filed
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2. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

3. ☒ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

see separate sheet

4. Additional observations, if necessary:

see separate sheet

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

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☐ the entire international application.

☒ claims Nos. 85-111.

because:

☒ the said international application, or the said claims Nos. 85-111 relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos. .

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

☐ restricted the claims.

☐ paid additional fees.

☐ paid additional fees under protest.

☒ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

☐ complied with.

☒ not complied with for the following reasons:

see separate sheet

4. Consequently, the following parts of the international application were the subject of international preliminary

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examination in establishing this report:

☐ all parts.

☒ the parts relating to claims Nos. 1-10, 12-14, 17-32, 34-36, 39-51, 53-55, 58-60, 62-64, 67-117 all partially.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims 1-10, 12-14, 17-32, 34-36, 39-51, 53-55, 58-60, 62-64, 67-117 (please see also separate sheet)
	No:	Claims ---
Inventive step (IS)	Yes:	Claims ---
	No:	Claims 1-10, 12-14, 17-32, 34-36, 39-51, 53-55, 58-60, 62-64, 67-117
Industrial applicability (IA)	Yes:	Claims 1-10, 12-14, 17-32, 34-36, 39-51, 53-55, 58-60, 62-64, 67-84, 112-117
	No:	Claims ---

2. Citations and explanations

see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US98/14679

Part I

- * The pages designated in "Basis of the report" with 57a and 57b correspond to the pages submitted as 57/1 and 57/2 by the applicant.

The sequence listings on pages 1-415 have been filed on the filing date of the application and are therefore considered to form part of the description (Rule 13ter.1(f) PCT).

Pages 57/1 and 57/2 which contain Table 5 do not have a basis in the originally filed documents and therefore contravene Art. 34(2)(b) PCT. Hence, the results presented in Table 5 have not been taken into consideration for establishing this report.

On the amended page of claims an obvious error in claim 3 has been corrected and hence the requirements of Art. 34(2)(b) are met. It should, however, be noticed that the format and pagination of the amended page of claims does not correspond to the original set of claims.

Part III

Claims 85-111 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Art. 34(4)(a)(i) PCT).

Part IV

The requirement of unity of invention is not complied with for the reasons set out in PCT/ISA forms 206 and 210.

The applicant has chosen to proceed with Invention 563 and therefore, claims 1-10, 12-14, 17-32, 34-36, 39-51, 53-55, 58-60, 62-64, 67-117 insofar as they relate to SEQ ID NO: 681 (SEQ 681) have been examined (Art. 34(3)(c) PCT).

Part V

a) Novelty and Inventive step

None of the available prior art documents discloses SEQ ID NO:681 or close mutants thereof. Therefore, claims 1-10, 12-14, 17-32, 34-36, 39-51, 53-55, 58-60, 62-64, 67-117 insofar as they explicitly refer to SEQ 681, would appear to be novel.

It should, however, be borne in mind that at present some claims explicitly relate to **fragments** of SEQ 681 which are in no way limited (see e.g. claim 2) or to **agents capable of binding** to SEQ 681 (see e.g. claim 1); as these features do not have a clear technical meaning, the novelty of these claims could be prejudiced by nucleic acids and peptides with quite different sequences. Therefore, no conclusive examination as to the novelty (Art. 33(2) PCT) of the claims is possible (See also Part VIII).

Even claims restricted to the exact SEQ 681 and e.g. corresponding peptides would not appear to meet the requirements of the PCT with respect to inventive step (Art. 33(3) PCT) for the following reasons. SEQ 681 is a nucleic acid which has apparently been isolated from cancer total RNA by the SEREX approach. It is, however, not disclosed in the application which tissue was the source for the RNA extraction. In the SEREX approach, a cDNA library is constructed from fresh tumour specimens, packaged into lambda-phage vectors and expressed recombinantly in Escherichia coli. Recombinant proteins are transferred on to nitrocellulose membranes, and identified as antigens by their reactivity with high-titer IgG antibodies present in the patient's serum (autologous serum) detected using an enzyme-conjugated secondary antibody specific for human IgG. Positive clones are subcloned to monoclonality, and the nucleotide sequence of the inserted DNA is determined. This approach is known from the prior art (see e.g. D1: PNAS, 92, 1995, 11810-11813). The antigens found by this method can be tumour-specific, overexpressed in tumours or they can even be cancer-independent autoantigens. Therefore, confirmation of a found antigen as being tumour-specific must be done by further experiments.

For SEQ 681, no properties at all are given in the description. Although the whole description states in very general terms that the found sequences are cancer-specific

there is not a single experiment given for SEQ 681 which could prove this property and rule out the possibility that SEQ 681 is any other autoantigen. It appears therefore, that SEQ 681 has been randomly selected out of a wealth of several hundred sequences identified by the applicant when applying a standard screening method. As it is not apparent whether SEQ 681 solves any technical problem, no inventive step can be acknowledged for any of the subject-matter examined.

b) Industrial Applicability

For the assessment of the present claims 85-111 on the question whether they are industrially applicable, no unified criteria exist in the PCT contracting states. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Part VII

- a) The expression "herein incorporated by reference" or equivalents thereof (see e.g. pages 5, 58 and 88) will have to be deleted in some cases when entering the national or regional phase (see e.g. the Guidelines for Examination in the EPO, C-II, 4.18)
- b) The reference to non-published patent applications (see e.g. pages 37 and 84) should be changed to published publication numbers throughout the application.
- c) Table 5 which is referred to in Example 6 (see page 57) of the description is missing, thereby leading to an inconsistency. It appears, however, that this inconsistency cannot be overcome without infringing Art. 34(2)(b) PCT (see also Part I).

Part VIII

- a) All claims examined are unclear as they include terms (NA group 1, PP group 1 etc.) which do not have an unambiguous meaning in the relevant art (Art. 6 PCT). Inclusion of the definitions for these groups given in the description (pages 13-16) would have remedied this defect; it appears that the definitions in the description are clear in scope as the fragments of the specific sequence to which the definitions relate are clearly limited by their function. However, several claims are additionally rendered unclear by explicitly relating to fragments which are not even functionally limited (see e.g. claim 2), Art. 6 PCT. This unclarity should have been overcome by deleting the unclear term.
- b) In the description of the present application it is not at all apparent from which cancer tissue the RNA leading to the detection of SEQ 681 has been extracted. Nevertheless, it appears that the information as to SEQ 681 given in the sequence listings is sufficient to put the skilled person into a position to perform the invention according to claims 1-84 and 112-117. The objection as to insufficient disclosure (Art. 5 PCT) is therefore dropped with regard to claims 1-84 and 112-117.

However, an objection as to lack of support applies to the methods of treating a patient (claims 85-111) since no methods of treatment are disclosed at all (Art. 6 PCT). Moreover, as neither the function and properties nor the tissue specificity of SEQ 681 are known (the description merely gives general statements and does nowhere explicitly mention SEQ 681 or a single experiment with this sequence), it is doubtful whether treatment could be performed with this nucleic acid sequence or corresponding peptides. Moreover, even if it could be clearly proven that SEQ 681 was a cancer restricted antigen, the success of treatment by protein vaccination (claims 85-89), provision of cytolytic T cells against the antigen (claims 90-92), DNA vaccination (claims 93-98) would be fully speculative. Although it is not questioned that the principles of the above methods are known in the art it should nevertheless be noticed that these methods only work under carefully selected conditions and there is no standard procedure. For these reasons, the skilled person could not perform the invention according to claims 85-111 without undue burden, contrary to Art. 5 PCT.